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L1: Entry 11 of 77

File: USPT

Mar 12, 2002

DOCUMENT-IDENTIFIER: US 6355268 B1

**** See image for Certificate of Correction ****

TITLE: Liposome-entrapped topoisomerase inhibitors

Detailed Description Text (83):

In another study performed in support of the invention, topotecan was entrapped in liposomes composed of DSPC and mPEG-DSPE in a 95:5 molar ratio, as described in Example 4. Early studies, not reported here, indicated that topotecan was not readily retained in the liposomes. The lipid bilayer was selected to use a single component phospholipid having an acyl chain length close to DSPE in the mPEG-DSPE component. Such a bilayer has minimal packing defects which arise from imperfections in nearest neighbor interactions in a solid phase bilayer, which have reduced lateral and rotational mobility relative to fluid bilayers. In addition, a dextran-sulfate loading battery was used in order to achieve precipitation of the topotecan in the liposome interior. Other polymers, in particular polyanionic polymers, are suitable for this purpose, such as chondroitin sulfate A, polyvinylsulfuric acid, and polyphosphoric acid.

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L1: Entry 12 of 77

File: USPT

Mar 12, 2002

DOCUMENT-IDENTIFIER: US 6355267 B1

**** See image for Certificate of Correction ****

TITLE: Liposome preparation and material encapsulation method

Detailed Description Text (68):

Liposomes (DPPC; DMPG:DSPC:CHOL; DSPC:CHOL) were prepared substantially in accordance with Method 4, above, to contain calcein, a self-quenching fluorescent dye (MW 622). The liposomes were diluted into 80% human serum and incubated at 37.degree. C. The final lipid concentration during the incubation was 6 mM. At the indicated times, aliquots of the samples were removed and diluted to 12 .mu.M (1:500) or less. Fluorescence was measured before (F) and after (F.sub.T) addition of Triton X-100 to a final concentration of 1%. The percent release was calculated as: %Release=100(F-F₀)/(F_T-F₀) where F₀ is the fluorescence at 0 time (or no serum).

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L1: Entry 20 of 77

File: USPT

Jul 18, 2000

DOCUMENT-IDENTIFIER: US 6090406 A

TITLE: Potentiation of immune responses with liposomal adjuvants

Brief Summary Text (108) :

The loading of liposomes with the peptide-like therapeutic agent is also enhanced by the use of stable lipids in the practice of this invention. For example, when liposomes entrapping BSTH were formed in the presence of lipid:BSTH at 2:1 (lipid:peptide) the liposomes thus formed were 6.1:1 lipid:peptide as opposed to 16.2:1 for similar liposomes formed from unhydrogenated lipids. In another instance liposomes prepared from lipid:galactose-albumin (1.8:1 feed) yielded a lipid:galactose-albumin liposome of 4.3:1 as opposed to 7.1:1 for unhydrogenated liposomes at a similar lipid:galactose-albumin feed ratio. In another example, DSPC liposomes (DSPC is obtainable from Avanti Polar Lipids, Birmingham, Ala.), optionally mixed with cholesterol (preferably 7:3 mole ratio of phospholipid to cholesterol), were formed entrapping calcitonin. Calcitonin is available in many forms and analogues and derivatives of calcitonin are being developed or are now available. All such analogues and derivatives are understood to be included in the term calcitonin. The high integrity liposomes of this invention extended the presence of detectable calcitonin from about 1 hour for free calcitonin to about 3 to 7 days.

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L1: Entry 46 of 77

File: USPT

Jun 16, 1998

DOCUMENT-IDENTIFIER: US 5766624 A

TITLE: Liposomal defensins

Drawing Description Text (9):

FIG. 7. Order Parameter of Liposomal Indolicidin Systems. The vertical axis shows the effect on the order parameter of various liposomal systems of the addition of indolicidin at increasing indolicidin concentrations (mole percent, horizontal axis) using the spin label 1-palmitoyl-2(12 doxyl stearoyl)-phosphatidylcholine at a concentration of 1 mole percent. Open squares: DPPC liposomes; open triangles: DSPC liposomes; open circles: DSPC/Chol (3:2) liposomes; asterisks: DHPC liposomes; filled squares: POPC liposomes; filled triangles: POPC/DOTAP (dioleoyl trimethylamino propane) (5:4:1) liposomes; filled circles: POPC/DOTAP (9:1) liposomes; and filled bars: DSPC/Chol/DDAB (dimethylamino dioctadecyl ammonium bromide) liposomes.

Detailed Description Text (11):

The liposome of this invention can be unilamellar or multilamellar, but is preferably multilamellar. Multiple lipid bilayers present a greater number of barriers to defensin release from liposomes. The multilamellar liposome can be an ordinary MLV, that is, an MLV produced by a process similar to that of Bangham et al. (J. Mol. Biol. 13:238 --dissolve amphipathic lipid(s) in an organic solvent, evaporate the solvent and then rehydrate the dried lipids with an aqueous medium). Such MLVs can be further processed. For example, POPC, indolicidin-containing liposomes can be prepared by preparing a mixture of indolicidin and POPC in one or more organic solvents (e.g., ethanol, methanol and chloroform), evaporating the organic solvent and hydrating the dried lipids with an aqueous buffer. The resultant liposomes are ordinary MLVs and can be extruded through filters of a defined pore size (e.g., five microns), to reduce their lamellarity and homogenize their size, according to the procedures of Cullis et al. (U.S. Pat. No. 5,008,050) and Loughrey et al. (U.S. Pat. No. 5,059,421). However, the multilamellar liposome of this invention preferably contains a solute entrapped in its aqueous compartments, wherein the concentration of the solute in each of the aqueous compartments is substantially equal, i.e., the multilamellar liposome has substantially equal interlamellar solute distribution. The liposome can, for example, be prepared with DSPC and cholesterol and can be more osmotically stable than an ordinary MLV.

Detailed Description Text (77):

The pH 5.3 and the pH 7.3 liposome samples were vortexed and then incubated at room temperature (POPC-containing liposomes: 10 minutes; DSPC/Chol-containing liposomes: 1 hour). A small aliquot of each sample was removed and set aside for use in a standard phosphate assay (see Chen et al., Anal. Chem. 28:1956 (1956)) to measure lipid concentration. Next, 200 .mu.l of a 1% polyaspartic acid solution was added to each tube, which were then allowed to stand for 10 minutes before the absorbance at 550 nm was recorded.

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L1: Entry 67 of 77

File: USPT

Jan 10, 1995

DOCUMENT-IDENTIFIER: US 5380531 A

TITLE: Accumulations of amino acids and peptides into liposomes

Detailed Description Text (28) :

In the present invention, the preferred liposomes are those which are unilamellar liposomes of about 0.1 to about 0.2 microns. As described hereinabove, a number of lipids may be used to form liposomes having a gel to liquid crystalline Tc above ambient temperature. In such cases, an extruder having a heating barrel or thermojacket may be employed. Such a device serves to increase the liposome suspension temperature allowing extrusion of the LUVs. The lipids which are used with the thermojacketed extruder are, for example, DSPC, DPPC, DMPC and DAPC or mixtures thereof, which may include cholesterol in certain embodiments for preventing the rapid release of agents from the liposome. Liposomes containing DSPC are generally extruded at about 65.degree. C., DPPC at about 45.degree. C. and DAPC at about 85.degree. C. (about 5.degree. C. above the lipid T.sub.c).

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L1: Entry 71 of 77

File: USPT

Oct 22, 1991

DOCUMENT-IDENTIFIER: US 5059421 A

TITLE: Preparation of targeted liposome systems of a defined size distribution

Detailed Description Text (27):

As described hereinabove, a number of lipids may be used to form reactive liposomes having a gel to liquid crystalline T_{sub}c above ambient temperature. In such cases, an extruder having a heating barrel or thermojacket may be employed. Such a device serves to increase the liposome suspension temperature allowing extrusion of the LUVs. The lipids which are used with the thermojacketed extruder are, for example, DSPC, DPPC, DMPC and DAPC or mixtures thereof, which may include cholesterol in certain embodiments. Liposomes containing DSPC are generally extruded at about 65.degree. C., DPPC at about 45.degree. C. and DAPC at about 85.degree. C. (about 5.degree. C. above the lipid T_{sub}c).

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L1: Entry 72 of 77

File: USPT

May 7, 1991

DOCUMENT-IDENTIFIER: US 5013556 A

TITLE: Liposomes with enhanced circulation time

Brief Summary Text (41):

One approach which has been proposed is to increase liposome circulation time by increasing liposome stability in serum. This approach is based on studies which have shown that factors which decrease leakage of liposome contents in plasma also decrease the rate of uptake of liposomes by the RES (Allen, 1983; Gregoriadis, 1980; Allen, 1981; Senior, 1982). One factor contributing to this effect appears to be bilayer rigidity, which renders the liposomes more resistant to the destabilizing effects of serum components, in particular high density lipoproteins (Allen, 1981; Scherphof). Thus, inclusion of cholesterol in the liposomal bilayer can reduce the rate of uptake by the RES (Gregoriadis, 1980; Hwang; Senior, 1985), and solid liposomes such as those composed of distearoylphosphatidylcholine (DSPC) or containing large amounts of sphingomyelin (SM) show decreased rate and extent of uptake into liver (Allen, 1983; Ellens; Senior, 1982; Hwang). However, this approach appears to have a limited potential for increasing liposome circulation times in the bloodstream.

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L1: Entry 75 of 77

File: USPT

Apr 24, 1990

DOCUMENT-IDENTIFIER: US 4920016 A

** See image for Certificate of Correction **

TITLE: Liposomes with enhanced circulation time

Brief Summary Text (40):

One approach which has been proposed is to increase liposome circulation time by increasing liposome stability in serum. This approach is based on studies by one of the inventors and others which have shown that factors which decrease leakage of liposome contents in plasma also decrease the rate of uptake of liposomes by the RES (Allen, 1983; Gregoriadis, 1980; Allen, 1981; Senior, 1982). The most important factor contributing to this effect appears to be bilayer rigidity, which renders the liposomes more resistant to the destabilizing effects of serum components, in particular high density lipoproteins (Allen, 1981; Scherphof). Thus, inclusion of cholesterol in the liposomal bilayer can reduce the rate of uptake by the RES (Gregoriadis, 1980; Hwang; Patel, 1983; Senior, 1985), and solid liposomes such as those composed of distearoylphosphatidylcholine (DSPC) or containing large amounts of sphingomyelin (SM) show decreased rate and extent of uptake into liver (Allen, 1983; Ellens; Senior, 1982; Hwang).

Detailed Description Text (18):

FIGS. 2A and 2B are plots of blood/RES values as a function of GM.sub.1 mole ratio in two different liposome formulations. The first, shown in FIG. 2A, is a PC:CH formulation (which gives suboptimal blood/RES ratios), and the second, an SM:PC formulation. As discussed in Example 6, only the latter formulation shows a strong GM.sub.1 effect. As seen, the optimal concentration of GM.sub.1 is between 5-15 mole percent. The effect of high glycolipid concentration on blood/RES ratios is seen in Example 10, which examines 4 and 24 hour blood/RES ratios for liposomes containing DSPC:CH or PC:CH and increasing molar concentrations of HPI. Molar ratios of HPI above about 25% substantially eliminated the enhanced blood/RES values seen at concentrations of about 16 mole percent or below.

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L4: Entry 25 of 26

File: USPT

May 25, 1993

DOCUMENT-IDENTIFIER: US 5213804 A

** See image for Certificate of Correction **

TITLE: Solid tumor treatment method and composition

Detailed Description Text (220):

Two groups of 6 mice were injected subcutaneously with 10.sup.5 -10.sup.6 C-26 colon carcinoma cells and the tumor was allowed to grow in the subcutaneous space until it reached a size of about 1 cm.sup.3 (about two weeks following injection). Each group of animals was then injected with 0.5 mg of either conventional liposomes (100 nm DSPC/Chol, 1:1) or PEG liposomes (100 nm DSPC/Chol/PEG-DSPE, 10:3:1) which had been loaded with radioactive gallium as described in Example 4. Three mice from each group were sacrificed at 2, 24 and 48 hours post treatment, the tumors excised and weighed and the amount of radioactivity quantified using a gamma counter. The results are presented in the following table and are expressed as the percent of the injected dose per gram tissue.

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